



General

Guideline Title

Hyperthyroidism and other causes of thyrotoxicosis: management guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists.

Bibliographic Source(s)

Bahn Chair RS, Burch HB, Cooper DS, Garber JR, Greenlee MC, Klein I, Laurberg P, McDougall IR, Montori VM, Rivkees SA, Ross DS, Sosa JA, Stan MN, American Thyroid Association, American Association of Clinical Endocrinologists. Hyperthyroidism and other causes of thyrotoxicosis: management guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists. *Thyroid*. 2011 Jun;21(6):593-646. [358 references] [PubMed](#)

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Definitions for the strength of the recommendations (1, 2) and quality of the evidence (+++, ++0, +00) are presented at the end of the "Major Recommendations" field.

How Should Clinically or Incidentally Discovered Thyrotoxicosis Be Evaluated and Initially Managed?

R1. A radioactive iodine uptake should be performed when the clinical presentation of thyrotoxicosis is not diagnostic of Graves' Disease (GD); a thyroid scan should be added in the presence of thyroid nodularity. 1/+00

R2. Beta-adrenergic blockade should be given to elderly patients with symptomatic thyrotoxicosis and to other thyrotoxic patients with resting heart rates in excess of 90 beats per minute or coexistent cardiovascular disease. 1/++0

R3. Beta-adrenergic blockade should be considered in all patients with symptomatic thyrotoxicosis. 1/+00

How Should Overt Hyperthyroidism Due to GD Be Managed?

R4. Patients with overt Graves' hyperthyroidism should be treated with any of the following modalities: ¹³¹I therapy, antithyroid medication, or thyroidectomy. 1/++0

If ¹³¹I Therapy Is Chosen as Treatment for GD, How Should It Be Accomplished?

R5. Patients with GD who are at increased risk for complications due to worsening of hyperthyroidism (i.e., those who are extremely symptomatic or have free thyroxine (T₄) estimates 2–3 times the upper limit of normal) should be treated with beta-adrenergic blockade prior to radioactive iodine therapy. 1/+00

R6. Pretreatment with methimazole prior to radioactive iodine therapy for GD should be considered in patients who are at increased risk for complications due to worsening of hyperthyroidism (i.e., those who are extremely symptomatic or have free T₄ estimate 2–3 times the upper limit of normal). 2/+00 (*Task force opinion was not unanimous; one person held the opinion that pretreatment with methimazole is not necessary in this setting.*)

R7. Medical therapy of any comorbid conditions should be optimized prior to administering radioactive iodine. 1/+00

R8. Sufficient radiation should be administered in a single dose (typically 10–15 mCi) to render the patient with GD hypothyroid. 1/++0

R9. A pregnancy test should be obtained within 48 hours prior to treatment in any female with childbearing potential who is to be treated with radioactive iodine. The treating physician should obtain this test and verify a negative result prior to administering radioactive iodine. 1/+00

R10. The physician administering the radioactive iodine should provide written advice concerning radiation safety precautions following treatment. If the precautions cannot be followed, alternative therapy should be selected. 1/+00

R11. Follow-up within the first 1–2 months after radioactive iodine therapy for GD should include an assessment of free T₄ and total triiodothyronine (T₃). If the patient remains thyrotoxic, biochemical monitoring should be continued at 4– to 6-week intervals. 1/+00

R12. When hyperthyroidism due to GD persists after 6 months following ¹³¹I therapy, or if there is minimal response 3 months after therapy, retreatment with ¹³¹I is suggested. 2/+00

If Antithyroid Drugs Are Chosen as Initial Management of GD, How Should the Therapy Be Managed?

R13. Methimazole should be used in virtually every patient who chooses antithyroid drug therapy for GD, except during the first trimester of pregnancy when propylthiouracil is preferred, in the treatment of thyroid storm, and in patients with minor reactions to methimazole who refuse radioactive iodine therapy or surgery. 1/++0

R14. Patients should be informed of side effects of antithyroid drugs and the necessity of informing the physician promptly if they should develop pruritic rash, jaundice, acolic stools or dark urine, arthralgias, abdominal pain, nausea, fatigue, fever, or pharyngitis. Before starting antithyroid drugs and at each subsequent visit, the patient should be alerted to stop the medication immediately and call their physician when there are symptoms suggestive of agranulocytosis or hepatic injury. 1/+00

R15. Prior to initiating antithyroid drug therapy for GD, the task force suggests that patients have a baseline complete blood count, including white count with differential, and a liver profile including bilirubin and transaminases. 2/+00

R16. A differential white blood cell count should be obtained during febrile illness and at the onset of pharyngitis in all patients taking antithyroid medication. Routine monitoring of white blood counts is not recommended. 1/+00

R17. Liver function and hepatocellular integrity should be assessed in patients taking propylthiouracil who experience pruritic rash, jaundice, light colored stool or dark urine, joint pain, abdominal pain or bloating, anorexia, nausea, or fatigue. 1/+00

R18. Minor cutaneous reactions may be managed with concurrent antihistamine therapy without stopping the antithyroid drug. Persistent minor side effects of antithyroid medication should be managed by cessation of the medication and changing to radioactive iodine or surgery, or switching to the other antithyroid drug when radioactive iodine or surgery are not options. In the case of a serious allergic reaction, prescribing the alternative drug is not recommended. 1/+00

R19. If methimazole is chosen as the primary therapy for GD, the medication should be continued for approximately 12–18 months, then tapered or discontinued if the thyroid-stimulating hormone (TSH) is normal at that time. 1/+++

R20. Measurement of thyrotropin receptor antibody (TRAb) levels prior to stopping antithyroid drug therapy is suggested, as it aids in predicting which patients can be weaned from the medication, with normal levels indicating greater chance for remission. 2/+00

R21. If a patient with GD becomes hyperthyroid after completing a course of methimazole, consideration should be given to treatment with radioactive iodine or thyroidectomy. Low-dose methimazole treatment for longer than 12–18 months may be considered in patients not in remission who prefer this approach. 2/+00

If Thyroidectomy Is Chosen for Treatment of GD, How Should It Be Accomplished?

R22. Whenever possible, patients with GD undergoing thyroidectomy should be rendered euthyroid with methimazole. Potassium iodide should be given in the immediate preoperative period. 1/+00

R23. In exceptional circumstances, when it is not possible to render a patient with GD euthyroid prior to thyroidectomy, the need for thyroidectomy is urgent, or when the patient is allergic to antithyroid medication, the patient should be adequately treated with beta-blockade and potassium iodide in the immediate preoperative period. The surgeon and anesthesiologist should have experience in this situation. 1/+00

R24. If surgery is chosen as the primary therapy for GD, near-total or total thyroidectomy is the procedure of choice. 1/++0

R25. If surgery is chosen as the primary therapy for GD, the patient should be referred to a high volume thyroid surgeon. 1/++0

R26. Following thyroidectomy for GD, the task force suggests that serum calcium or intact parathyroid hormone levels be measured, and that oral calcium and calcitriol supplementation be administered based on these results. 2/+00

R27. Antithyroid drugs should be stopped at the time of thyroidectomy for GD, and beta-adrenergic blockers should be weaned following surgery. 1/+00

R28. Following thyroidectomy for GD, L-thyroxine should be started at a daily dose appropriate for the patient's weight (0.8 µgram/lb or 1.7 µgram/kg), and serum TSH measured 6–8 weeks postoperatively. 1/+00

How Should Thyroid Nodules Be Managed in Patients with GD?

R29. If a thyroid nodule is discovered in a patient with GD, the nodule should be evaluated and managed according to recently published guidelines regarding thyroid nodules in euthyroid individuals. 1/++0

How Should Thyroid Storm Be Managed?

R30. A multimodality treatment approach to patients with thyroid storm should be used, including beta-adrenergic blockade, antithyroid drug therapy, inorganic iodide, corticosteroid therapy, aggressive cooling with acetaminophen and cooling blankets, volume resuscitation, respiratory support and monitoring in an intensive care unit. 1/+00

How Should Overt Hyperthyroidism Due to Toxic Multinodular Goiter (TMNG) or Toxic Adenoma (TA) Be Treated?

R31. The task force suggests that patients with overtly TMNG or TA be treated with either ¹³¹I therapy or thyroidectomy. On occasion, long term, low-dose treatment with methimazole may be appropriate. 2/++0

If ¹³¹I Therapy Is Chosen as Treatment for TMNG or TA, How Should It Be Accomplished?

R32. Patients with TMNG or TA who are at increased risk for complications due to worsening of hyperthyroidism, including the elderly and those with cardiovascular disease or severe hyperthyroidism, should be treated with beta-blockade prior to radioactive iodine therapy and until euthyroidism has been achieved. 1/+00

R33. Pretreatment with methimazole prior to radioactive iodine therapy for TMNG or TA should be considered in patients who are at increased risk for complications due to worsening of hyperthyroidism, including the elderly and those with cardiovascular disease or severe hyperthyroidism. 2/+00 (*Task force opinion was not unanimous; one member held the opinion that pretreatment with methimazole in patients already treated with beta-adrenergic blockade is not indicated in this setting.*)

R34. Nonfunctioning nodules on radionuclide scintigraphy or nodules with suspicious ultrasound characteristics should be managed according to recently published guidelines regarding thyroid nodules in euthyroid individuals. 1/++0

R35. For radioactive iodine treatment of TMNG, sufficient radiation should be administered in a single dose to alleviate hyperthyroidism. 1/++0

R36. For radioactive iodine treatment of TA, sufficient radiation to alleviate hyperthyroidism should be administered in a single dose. 1/++0

R37. Follow-up within the first 1–2 months after radioactive iodine therapy for TMNG or TA should include an assessment of free T₄, total T₃ and TSH. This should be repeated at 1– to 2-month intervals until stable results are obtained, then at least annually thereafter according to clinical indication. 1/+00

R38. If hyperthyroidism persists beyond 6 months following ¹³¹I therapy for TMNG or TA, retreatment with radioactive iodine is suggested.

If Surgery Is Chosen for Treatment of TMNG or TA, How Should It Be Accomplished?

R39. If surgery is chosen as treatment for TMNG or TA, patients with overt hyperthyroidism should be rendered euthyroid prior to the procedure with methimazole pretreatment (in the absence of allergy to the medication), with or without beta-adrenergic blockade. Preoperative iodine should not be used in this setting. 1/+00

R40. If surgery is chosen as treatment for TMNG, near- total or total thyroidectomy should be performed. 1/++0

R41. Surgery for TMNG should be performed by a high-volume thyroid surgeon. 1/++0

R42. If surgery is chosen as the treatment for TA, an ipsilateral thyroid lobectomy, or isthmusectomy if the adenoma is in the thyroid isthmus, should be performed. 1/++0

R43. The task force suggests that surgery for TA be performed by a high-volume surgeon. 2/++0

R44. Following thyroidectomy for TMNG, the task force suggests that serum calcium or intact parathyroid hormone levels be measured, and that oral calcium and calcitriol supplementation be administered based on these results. 2/+00

R45. Methimazole should be stopped at the time of surgery for TMNG or TA. Beta-adrenergic blockade should be slowly discontinued following surgery. 1/+00

R46. Following surgery for TMNG, thyroid hormone replacement should be started at a dose appropriate for the patient's weight (0.8 µgram/lb or 1.7 µgram/kg) and age, with elderly patients needing somewhat less. TSH should be measured every 1–2 months until stable, and then annually. 1/+00

R47. Following surgery for TA, TSH and estimated free T4 levels should be obtained 4–6 weeks after surgery, and thyroid hormone supplementation started if there is a persistent rise in TSH above the normal range. 1/+00

R48. Radioactive iodine therapy should be used for retreatment of persistent or recurrent hyperthyroidism following inadequate surgery for TMNG or TA. 1/+00

Is There a Role for Antithyroid Drug Therapy in Patients with TMNG or TA?

R49. The task force suggests that long-term methimazole treatment of TMNG or TA be avoided, except in some elderly or otherwise ill patients with limited longevity who are able to be monitored regularly, and in patients who prefer this option. 2/+00

How Should GD Be Managed in Children and Adolescents?

R50. Children with GD should be treated with methimazole, ¹³¹I therapy, or thyroidectomy. ¹³¹I therapy should be avoided in very young children (<5 years). ¹³¹I therapy in patients between 5 and 10 years of age is acceptable if the calculated ¹³¹I administered activity is <10 mCi. ¹³¹I therapy in patients older than 10 years of age is acceptable if the activity is >150 µCi/g of thyroid tissue. Thyroidectomy should be chosen when definitive therapy is required, the child is too young for ¹³¹I, and surgery can be performed by a high-volume thyroid surgeon. 1/++0

If Antithyroid Drugs Are Chosen as Initial Management of GD in Children, How Should the Therapy Be Managed?

R51. Methimazole should be used in virtually every child who is treated with antithyroid drug therapy. 1/++0

R52. Pediatric patients and their caretakers should be informed of side effects of antithyroid drugs and the necessity of stopping the medication immediately and informing their physician if they develop pruritic rash, jaundice, acolic stools or dark urine, arthralgias, abdominal pain, nausea, fatigue, fever, or pharyngitis. 1/+00

R53. Prior to initiating antithyroid drug therapy, the task force suggests that pediatric patients have, as a baseline, complete blood cell count, including white blood cell count with differential, and a liver profile including bilirubin, transaminases, and alkaline phosphatase. 2/+00

R54. Beta-adrenergic blockade is recommended for children experiencing symptoms of hyperthyroidism, especially those with heart rates in excess of 100 beats per minute. 1/+00

R55. Antithyroid medication should be stopped immediately, and white blood counts measured in children who develop fever, arthralgias, mouth sores, pharyngitis, or malaise. 1/+00

R56. When propylthiouracil is used in children, the medication should be stopped immediately and liver function and hepatocellular integrity assessed in children who experience anorexia, pruritus, rash, jaundice, light-colored stool or dark urine, joint pain, right upper quadrant pain or abdominal bloating, nausea or malaise. 1/+00

R57. Persistent minor cutaneous reactions to methimazole therapy in children should be managed by concurrent antihistamine treatment or cessation of the medication and changing to therapy with radioactive iodine or surgery. In the case of a serious allergic reaction to an antithyroid medication, prescribing the other antithyroid drug is not recommended. 1/+00

R58. If methimazole is chosen as the first-line treatment for GD in children, it should be administered for 1–2 years and then discontinued, or the dose reduced, to assess whether the patient is in remission. 1/++0

R59. Pediatric patients with GD who are not in remission following 1–2 years of methimazole therapy should be considered for treatment with radioactive iodine or thyroidectomy. 1/+00

If Radioactive Iodine Is Chosen as Treatment for GD in Children, How Should It Be Accomplished?

R60. We suggest that children with GD having total T₄ levels of >20 µgrams/dL (260 nmol/L) or free T₄ estimates >5 ng/dL (60 pmol/L) who are to receive radioactive iodine therapy be pretreated with methimazole and beta-adrenergic blockade until total T₄ and/or free T₄ estimates normalize before proceeding with radioactive iodine. 2/+00

R61. If ¹³¹I therapy is chosen as treatment for GD in children, sufficient ¹³¹I should be administered in a single dose to render the patient hypothyroid. 1/++0

If Thyroidectomy Is Chosen as Treatment for GD in Children, How Should It Be Accomplished?

R62. Children with GD undergoing thyroidectomy should be rendered euthyroid with the use of methimazole. Potassium iodide should be given in the immediate preoperative period. 1/+00

R63. If surgery is chosen as therapy for GD in children, total or near-total thyroidectomy should be performed. 1/++0

R64. Thyroidectomy in children should be performed by high-volume thyroid surgeons. 1/++0

How Should Subclinical Hyperthyroidism (SH) Be Managed?

R65. When TSH is persistently <0.1 mU/L, treatment of SH should be strongly considered in all individuals 65 years of age and older, and in postmenopausal women who are not on estrogens or bisphosphonates; patients with cardiac risk factors, heart disease or osteoporosis; and individuals with hyperthyroid symptoms. 2/++0

R66. When TSH is persistently below the lower limit of normal but ≥0.1 mU/L, treatment of SH should be considered in individuals 65 years of age and older and in patients with cardiac disease or symptoms of hyperthyroidism. 2/+00

R67. If SH is to be treated, the treatment should be based on the etiology of the thyroid dysfunction and follow the same principles as outlined for the treatment of overt hyperthyroidism. 1/+00

How Should Hyperthyroidism in Pregnancy Be Managed?

R68. The diagnosis of hyperthyroidism in pregnancy should be made using serum TSH values, and either total T₄ and T₃ with total T₄ and T₃ reference range adjusted at 1.5 times the nonpregnant range or free T₄ and free T₃ estimations with trimester-specific normal reference ranges. 1/+00

R69. Transient human chorionic gonadotropin (hCG)-mediated thyrotropin suppression in early pregnancy should not be treated with antithyroid drug therapy. 1/+00

R70. Antithyroid drug therapy should be used for hyperthyroidism due to GD that requires treatment during pregnancy. Propylthiouracil should be used when antithyroid drug therapy is started during the first trimester. Methimazole should be used when antithyroid drug therapy is started after the first trimester. 1/+00

R71. The task force suggests that patients taking methimazole who decide to become pregnant obtain pregnancy testing at the earliest suggestion of pregnancy and be switched to propylthiouracil as soon as possible in the first trimester and changed back to methimazole at the beginning of the second trimester. Similarly, the task force suggests that patients started on propylthiouracil during the first trimester be switched to methimazole at

the beginning of the second trimester. 2/+00

R72. GD during pregnancy should be treated with the lowest possible dose of antithyroid drugs needed to keep the mother's thyroid hormone levels slightly above the normal range for total T₄ and T₃ values in pregnancy and the TSH suppressed. Free T₄ estimates should be kept at or slightly above the upper limit of the nonpregnant reference range. Thyroid function should be assessed monthly, and the antithyroid drug dose adjusted as required. 1/+00

R73. When thyroidectomy is necessary for the treatment of hyperthyroidism during pregnancy, the surgery should be performed if possible during the second trimester. 1/+00

R74. TRAb levels should be measured when the etiology of hyperthyroidism in pregnancy is uncertain. 1/+00

R75. Patients who were treated with radioactive iodine or thyroidectomy for GD prior to pregnancy should have TRAb levels measured using a sensitive assay either initially at 22–26 weeks of gestation, or initially during the first trimester and, if elevated, again at 22–26 weeks of gestation. 1/+00

R76. Patients found to have GD during pregnancy should have TRAb levels measured at diagnosis using a sensitive assay and, if elevated, again at 22–26 weeks of gestation. 1/+00

R77. TRAb levels measured at 22–26 weeks of gestation should be used to guide decisions regarding neonatal monitoring. 1/+00

R78. In women with thyrotoxicosis after delivery, selective diagnostic studies should be performed to distinguish postpartum thyroiditis from postpartum GD. 1/+00

R79. In women with symptomatic postpartum thyrotoxicosis, the judicious use of beta-adrenergic blocking agents is recommended. 1/+00

How Should Hyperthyroidism Be Managed in Patients with Graves' Ophthalmopathy?

R80. Euthyroidism should be expeditiously achieved and maintained in hyperthyroid patients with Graves' ophthalmopathy or risk factors for the development of ophthalmopathy. 1/++0

R81. In nonsmoking patients with Graves' hyperthyroidism who have no clinically apparent ophthalmopathy, ¹³¹I therapy without concurrent steroids, methimazole or thyroidectomy should be considered equally acceptable therapeutic options. 1/++0

R82. Clinicians should advise patients with GD to stop smoking and refer them to a structured smoking cessation program. Patients exposed to secondhand smoke should be identified and advised of its negative impact. 1/++0

R83. In patients with Graves' hyperthyroidism who have mild active ophthalmopathy and no risk factors for deterioration of their eye disease, ¹³¹I therapy, methimazole, and thyroidectomy should be considered equally acceptable therapeutic options. 1/++0

R84. Patients with Graves' hyperthyroidism and mild active ophthalmopathy who have no other risk factors for deterioration of their eye disease and choose radioactive iodine therapy should be considered for concurrent treatment with corticosteroids. 2/++0

R85. Patients with Graves' hyperthyroidism and mild active ophthalmopathy who are smokers or have other risk factors for Graves' ophthalmopathy and choose radioactive iodine therapy should receive concurrent corticosteroids. 1/++0

R86. Patients with Graves' hyperthyroidism and active moderate-to-severe or sight-threatening ophthalmopathy should be treated with either methimazole or surgery. 1/+00

R87. In patients with Graves' hyperthyroidism and inactive ophthalmopathy, the task force suggests that ¹³¹I therapy without concurrent corticosteroids, methimazole, and thyroidectomy are equally acceptable therapeutic options. 2/++0

How Should Overt Drug-Induced Thyrotoxicosis Be Managed?

R88. Beta-adrenergic blocking agents alone or in combination with methimazole should be used to treat overt iodine-induced hyperthyroidism. 1/+00

R89. Patients who develop thyrotoxicosis during therapy with interferon-alpha or interleukin-2 should be evaluated to determine etiology (thyroiditis vs. GD) and treated accordingly. 1/+00

R90. The task force suggests monitoring thyroid function tests before and at 1 and 3 months following the initiation of amiodarone therapy, and at

3– to 6-month intervals thereafter. 2/+00

R91. The task force suggests testing to distinguish type 1 (iodine-induced) from type 2 (thyroiditis) varieties of amiodarone-induced thyrotoxicosis. 1/+00

R92. The decision to stop amiodarone in the setting of thyrotoxicosis should be determined on an individual basis in consultation with a cardiologist, based on the presence or absence of effective alternative antiarrhythmic therapy. 1/+00

R93. Methimazole should be used to treat type 1 amiodarone-induced thyrotoxicosis and corticosteroids should be used to treat type 2 amiodarone-induced thyrotoxicosis. 1/+00

R94. Combined antithyroid drug and anti-inflammatory therapy should be used to treat patients with overt amiodarone-induced thyrotoxicosis who fail to respond to single modality therapy, and patients in whom the type of disease cannot be unequivocally determined. 1/+00

R95. Patients with amiodarone-induced thyrotoxicosis who are unresponsive to aggressive medical therapy with methimazole and corticosteroids should undergo thyroidectomy. 1/+00

How Should Thyrotoxicosis Due to Destructive Thyroiditis Be Managed?

R96. Patients with mild symptomatic subacute thyroiditis should be treated initially with beta-adrenergic- blocking drugs and nonsteroidal anti-inflammatory agents. Those failing to respond or those with moderate-to-severe symptoms should be treated with corticosteroids. 1/+00

How Should Thyrotoxicosis Due to Unusual Causes Be Managed?

R97. The diagnosis of TSH-secreting pituitary tumor should be based on an inappropriately normal or elevated serum TSH level associated with elevated free T₄ estimates and T₃ concentrations, usually associated with the presence of a pituitary tumor on magnetic resonance imaging (MRI) and the absence of a family history or genetic testing consistent with thyroid hormone resistance in a thyrotoxic patient. 1/+00

R98. Patients with TSH-secreting pituitary adenomas should undergo surgery performed by an experienced pituitary surgeon. 1/+00

R99. Patients with struma ovarii should be treated initially with surgical resection. 1/+00

R100. Treatment of hyperthyroidism due to choriocarcinoma should include both methimazole and treatment directed against the primary tumor. 1/+00

Definitions:

Grading of Recommendations, Assessment, Development, and Evaluation System

| Type of Grading | Definition of Grades |
|--------------------------------|---|
| Strength of the Recommendation | 1 = Strong recommendation (for or against) Applies to most patients in most circumstances Benefits clearly outweigh the risk (or vice versa) 2 = Weak recommendation (for or against) Best action may differ depending on circumstances or patient values Benefits and risks or burdens are closely balanced, or uncertain |
| Quality of the Evidence | +++ = High quality; evidence at low risk of bias, such as high quality randomized trials showing consistent results directly applicable to the recommendation ++0 = Moderate quality; studies with methodological flaws, showing inconsistent or indirect evidence +00 = Low quality; case series or unsystematic clinical observations |

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Hyperthyroidism and other causes of thyrotoxicosis including:

- Graves' disease
- Toxic multinodular goiter
- Toxic adenoma

Guideline Category

Diagnosis

Evaluation

Management

Treatment

Clinical Specialty

Endocrinology

Family Practice

Internal Medicine

Nuclear Medicine

Obstetrics and Gynecology

Ophthalmology

Otolaryngology

Pediatrics

Surgery

Intended Users

Advanced Practice Nurses

Physician Assistants

Physicians

Guideline Objective(s)

- To combine the best scientific evidence with the experience of seasoned clinicians and the pragmatic realities inherent in implementation
- To describe evidence-based clinical guidelines for the management of thyrotoxicosis that would be useful to generalist and subspecialty physicians and others providing care for patients with this condition

Target Population

Patients (adults and children) with suspected and/or confirmed thyrotoxicosis

Interventions and Practices Considered

Evaluation

1. Radioactive iodine uptake
2. Thyroid scan
3. History and physical exam

Management

1. Beta-adrenergic blockade
2. ^{131}I therapy
3. Antithyroid medication (methimazole, propylthiouracil)
4. Thyroidectomy
5. Pregnancy test prior to treatment in any female with childbearing potential who is to be treated with radioactive iodine
6. Provision of written advice concerning radiation safety precautions to patients
7. Follow-up measurement of free thyroxine (T_4) and total triiodothyronine (T_3)
8. Patient education on potential side effects of drug therapy
9. Baseline complete blood count (including white count with differential) and liver profile including bilirubin and transaminases before beginning antithyroid drugs
10. Management of side effects of therapy
11. Rendering of patients with Graves' disease euthyroid with methimazole prior to thyroidectomy
12. Oral calcium and calcitriol supplementation following thyroidectomy
13. Thyroid hormone replacement therapy following thyroidectomy
14. Management of thyroid storm using a multimodality approach
15. Management of thyroid nodules according to established guidelines
16. Management of Graves' disease in children, adolescents, and pregnant patients
17. Management of subclinical hyperthyroidism
18. Management of hyperthyroidism in patients with Graves' ophthalmopathy
19. Management of other miscellaneous causes of thyrotoxicosis

Major Outcomes Considered

- Sensitivity and specificity of diagnostic tests to evaluate thyrotoxicosis
- Serum thyroid hormone levels
- Remission rates
- Patient preferences with respect to treatment of thyrotoxicosis
- Safety, effectiveness, and possible side effects of treatments
- Patient surgical outcomes

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

To develop a scholarly and useful document, the task force first developed a list of the most common causes of thyrotoxicosis and the most important questions that a practitioner might pose when caring for a patient with a particular form of thyrotoxicosis or special clinical condition. Two task force members (primary discussants) were assigned to review the literature relevant to each of the topics, using a systematic PubMed search for primary references and reviews supplemented with additional published materials available before June 2010, and draft preliminary recommendations based on the literature and expert opinion where appropriate.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Quality of the Evidence

+++ = High quality; evidence at low risk of bias, such as high quality randomized trials showing consistent results directly applicable to the recommendation

++0 = Moderate quality; studies with methodological flaws, showing inconsistent or indirect evidence

+00 = Low quality; case series or unsystematic clinical observations

Methods Used to Analyze the Evidence

Review

Review of Published Meta-Analyses

Description of the Methods Used to Analyze the Evidence

The literature and recommendations suggested by the primary discussants were reviewed and discussed by the group at large. The process resulted in the development of the final recommendations and text.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The American Thyroid Association (ATA) Executive Council and the Executive Committee of the American Association of Clinical Endocrinologists (AACE) forged an agreement outlining the working relationship between the two groups surrounding the development and dissemination of management guidelines for the treatment of patients with thyrotoxicosis. A chairperson was selected to lead the task force and this individual identified the other 11 members of the panel in consultation with the ATA and the AACE boards of directors. Membership on the panel was based on clinical expertise, scholarly approach, and representation of adult and pediatric endocrinology, nuclear medicine, and surgery. The task force included individuals from both North America and Europe. In addition, the group recruited an expert on the development of evidence-based guidelines to serve in an advisory capacity.

A preliminary document and a series of recommendations concerning all of the topics were generated by each task force subgroup and then critically reviewed by the task force at large. The panel agreed recommendations would be based on consensus of the panel and that voting would be used if agreement could not be reached. Two recommendations were not unanimous and the dissenting position is noted in the recommendations. Task force deliberations took place during several lengthy committee meetings, multiple telephone conference calls, and through electronic communication.

These guidelines were developed to combine the best scientific evidence with the experience of seasoned clinicians and the pragmatic realities inherent in implementation. The task force elected to rate the recommendations according to the system developed by the Grading of Recommendations, Assessment, Development, and Evaluation Group, with a modification in the grading of evidence. Although the rating system chosen differs from those used in previous ATA and AACE clinical practice guidelines, the approach conforms with the recently updated AACE protocol for standardized production of clinical practice guidelines. The balance between benefits and risks, quality of evidence, applicability, and certainty of the baseline risk are all considered in judgments about the strength of recommendations (see the "Rating Scheme for the Strength of the Recommendations" field).

The risks and benefits or burdens associated with a weak recommendation are closely balanced or uncertain and the statement is generally associated with the phrase "the task force suggests" or "should be considered."

Rating Scheme for the Strength of the Recommendations

Strength of Recommendation

1 = Strong recommendation (for or against)

Applies to most patients in most circumstances

Benefits clearly outweigh the risk (or vice versa)

2 = Weak recommendation (for or against)

Best action may differ depending on circumstances or patient values

Benefits and risks or burdens are closely balanced, or uncertain

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The final document was approved by the American Thyroid Association (ATA) and American Association of Clinical Endocrinologists (AACE) on March 15, 2011 and officially endorsed (in alphabetical order) by American Academy of Otolaryngology– Head and Neck Surgery, Associazione Medici Endocrinologi, British Association of Endocrine and Thyroid Surgeons, Canadian Paediatric Endocrine Group–Groupe Canadien d'Endocrinologie Pédiatrique (endorsement of pediatric section only), European Association of Nuclear Medicine, The Endocrine Society, European Society of Endocrinology, European Society of Endocrine Surgeons, European Thyroid Association, International Association of Endocrine Surgeons, Latin American Thyroid Society, Pediatric Endocrine Society, Italian Endocrine Society, and Society of Nuclear Medicine.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Improved diagnosis and care of patients with thyrotoxicosis
- Improved patient outcome has been shown to be independently associated with high thyroidectomy surgeon volume; specifically, complication rate, length of hospital stay, and cost are reduced when the operation is performed by a surgeon who conducts many thyroidectomies

Potential Harms

- Systemic side effects of drug therapies including agranulocytosis and hepatotoxicity
- Cutaneous or other allergic reactions to diagnostic tests or drug therapies
- Surgical complications
- Radioactive iodine is excreted by saliva, urine, and stool. Significant radioactivity is retained within the thyroid for several days. It is therefore important that patients and families be informed of and adhere to local radiation safety recommendations following ^{131}I therapy.
- ^{131}I is widely used in children, but still viewed as controversial by some practitioners owing primarily to concern over cancer risks. Although there are sparse clinical data relating to radioactive iodine use in children with Graves' disease and subsequent thyroid cancer, it is known that risks of thyroid cancer after external irradiation are highest in children <5 years of age, and they decline with advancing age; see discussion of ^{131}I therapy and cancer risk in the original guideline document.

Contraindications

Contraindications

- *^{131}I therapy*: Definite contraindications include pregnancy, lactation, coexisting thyroid cancer, or suspicion of thyroid cancer, individuals unable to comply with radiation safety guidelines and females planning a pregnancy within 4–6 months.
- *Antithyroid drugs (ATDs)*:
 - Definite contraindications to long-term ATD therapy include previous known major adverse reactions to ATDs.
 - Baseline absolute neutrophil count $<500/\text{mm}^3$ or liver transaminase enzyme levels elevated more than fivefold the upper limit of normal are contraindications to initiating antithyroid drug therapy.
 - In a patient developing agranulocytosis or other serious side effects while taking either methimazole (MMI) or propylthiouracil (PTU), use of the other medication is absolutely contraindicated owing to risk of cross-reactivity between the two medications.
- *Surgery*: Factors that may mitigate against the choice of surgery include substantial comorbidity such as cardiopulmonary disease, end-stage cancer, or other debilitating disorders. Pregnancy is a relative contraindication and should only be used in this circumstance, when rapid control of hyperthyroidism is required and antithyroid medications cannot be used. Thyroidectomy is best avoided in the first and third trimesters of pregnancy because of teratogenic effects associated with anesthetic agents and increased risk of fetal loss in the first trimester and increased risk of preterm labor in the third. Optimally, thyroidectomy is performed in the latter portion of the second trimester. Although it is the safest time, it is not without risk (4.5%–5.5% risk of preterm labor).
- *Beta-blockers*: Since there is not sufficient beta-1 selectivity of the available beta-blockers at the recommended doses, these drugs are generally contraindicated in patients with bronchospastic asthma. However, in patients with quiescent bronchospastic asthma in whom heart rate control is essential, or in patients with mild obstructive airway disease or symptomatic Raynaud's phenomenon, a nonselective beta-blocker such as nadolol can be used cautiously, with careful monitoring of pulmonary status.

Qualifying Statements

Qualifying Statements

In this document, the task force outlines what they believe is current, rational, and optimal medical practice. It is not the intent of these guidelines to replace clinical judgment, individual decision making, or the wishes of the patient or family. Rather, each recommendation should be evaluated in light of these elements in order that optimal patient care is delivered. In some circumstances, it may be apparent that the level of care required may be best provided in centers where there is specific expertise, and that referral to such centers should be considered.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Foreign Language Translations

Patient Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Bahn Chair RS, Burch HB, Cooper DS, Garber JR, Greenlee MC, Klein I, Laurberg P, McDougall IR, Montori VM, Rivkees SA, Ross DS, Sosa JA, Stan MN, American Thyroid Association, American Association of Clinical Endocrinologists. Hyperthyroidism and other causes of thyrotoxicosis: management guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists. *Thyroid*. 2011 Jun;21(6):593-646. [358 references] [PubMed](#)

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2011 Jun

Guideline Developer(s)

American Association of Clinical Endocrinologists - Medical Specialty Society

American Thyroid Association - Professional Association

Source(s) of Funding

Funding for the guidelines was derived solely from the general funds of the American Thyroid Association and thus the task force functioned without commercial support.

Guideline Committee

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Financial Disclosures/Conflicts of Interest

Disclosure Information for 2 years before May 2010 and the known future as of May 2010: D.R. is a consultant for Abbott Laboratories and has received research grant support from Genzyme. For all other authors, no competing financial interests exist.

Panel members declared whether they had any potential conflict of interest at the initial meeting of the group and periodically during the course of deliberations. Funding for the guidelines was derived solely from the general funds of the American Thyroid Association (ATA) and thus the task force functioned without commercial support.

Guideline Endorser(s)

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Associazione Medici Endocrinologi - Medical Specialty Society

British Association of Endocrine and Thyroid Surgeons (BAETS) - Medical Specialty Society

Canadian Pediatric Endocrine Group--Groupe Canadien d'Endocrinologie Pédiatrique - Medical Specialty Society

European Association of Nuclear Medicine - Medical Specialty Society

European Society of Endocrine Surgeons - Professional Association

European Society of Endocrinology - Medical Specialty Society

European Thyroid Association - Disease Specific Society

International Association of Endocrine Surgeons - Professional Association

Italian Endocrine Society - Medical Specialty Society

Latin American Thyroid Society - Disease Specific Society

Pediatric Endocrine Society - Medical Specialty Society

Society of Nuclear Medicine and Molecular Imaging - Medical Specialty Society

The Endocrine Society - Professional Association

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the [American Thyroid Association Web site](#) .

Print copies: Available from American Thyroid Association, 6066 Leesburg Pike, Suite 550, Falls Church, VA 22041.

Availability of Companion Documents

None available

Patient Resources

The following are available:

- Hyperthyroidism. Web brochure. Available online or in Portable Document Format (PDF) from the [American Thyroid Association \(ATA\) Web site](#) . Also available in Spanish from the [ATA Web site](#) .
- Graves' disease. Web brochure. Available online or in Portable Document Format (PDF) from the [American Thyroid Association \(ATA\) Web site](#) . Also available in Spanish from the [ATA Web site](#) .

Additional patient education brochures are available from the [ATA Web site](#) .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI Institute on June 26, 2012. The information was verified by the guideline developer on June 28, 2012. This summary was updated by ECRI Institute on October 28, 2013 following the U.S. Food and Drug Administration advisory on Acetaminophen. This summary was updated by ECRI Institute on September 18, 2015 following the U.S. Food and Drug Administration advisory on non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs).

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